

Non surgical treatment of empyema thoracis with intrapleural streptokinase in a patient with AIDS

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Abstract

After unsuccessful treatment with intercostal tube drainage and antibiotics intrapleural streptokinase was used to treat successfully an empyema in a man with AIDS and advanced cutaneous Kaposi's sarcoma who was unfit for surgical decortication. The role of this technique in the management of HIV positive patients with empyema is discussed.

(*Genitourin Med* 1995;71:259-261)

Keywords: empyema; AIDS; streptokinase

Introduction

Bacterial infection, including pneumonia, is seen with increased frequency in patients infected with the human immunodeficiency virus (HIV).¹ Patients with bacterial pneumonia have an increased risk of complications, including empyema thoracis (pus in the pleural space).² Failure of conventional first line therapy, namely intercostal tube drainage and antibiotic, occurs when pleural fluid is no longer free flowing.³ Inadequate drainage is usually associated with the fibrinopurulent stage of the empyema process in which empyema fluid becomes multi loculated by the formation of fibrin strands. Fibrin deposition within the pleural cavity may take only a few days so patients may present with multi loculated effusions which are not amenable to tube drainage alone and surgery under general anaesthetic with open thorocotomy and chest tube placement or pleural decortication may be necessary.⁴ In an attempt to facilitate drainage and obviate the need for surgery enzymatic debridement of the pleural cavity with streptokinase is a non-invasive therapeutic option. Intrapleural instillation of streptokinase was first described in 1949.⁵ Its use did not become widespread because of the rare occurrence of intrapleural haemorrhage and systemic fibrinolysis.^{6,7} With the availability of purer fibrinolytic formulations there has been resurgence in the use of intrapleural fibrinolytic therapy.⁸

We report here an HIV positive man with advanced cutaneous Kaposi's sarcoma in whom first line therapy for empyema had failed and who was too sick for surgery. Intrapleural streptokinase successfully drained the empyema. This is the first documented use of this technique in a patient with AIDS.

Case report

A 33 year old Caucasian homosexual catering assistant first presented to the out-patients in April 1993 with widespread cutaneous and palatal Kaposi's sarcoma. Investigations at this time showed him to be HIV-1 antibody positive and the CD4 count was $0.07 \times 10^9/l$ (normal range = $0.35-2.2 \times 10^9/l$). He began primary prophylaxis against pneumocystis pneumonia with co-trimoxazole and also began zidovudine. Because of increasing facial and groin oedema cyclical chemotherapy was begun in July 1993 with vincristine 2 mg and bleomycin 30 mg each given IV once every three weeks. Having completed six cycles of chemotherapy many new cutaneous lesions appeared over the abdomen and groins and so liposomal doxorubicin was begun (35 mg IV given once every three weeks). This had a dramatic effect on the skin lesions. After four cycles a chest radiograph showed normal lung fields but a small left pleural effusion. In the absence of respiratory symptoms and fever the effusion was ascribed to Kaposi's sarcoma.

The patient was admitted to hospital in February 1994 complaining of tiredness and breathlessness of two weeks duration with a non productive cough for the last 48 hours. Examination revealed him to be clinically anaemic with a pyrexia of $38.8^\circ C$. Auscultation of the chest revealed an impaired percussion note at both bases but no crackles were heard. Investigations revealed Hb = 8.1 g/dl with a normochromic normocytic film, WBC = 1.8 (neutrophils = 1.0) $\times 10^9/l$ and a normal platelet count. Urea and electrolyte estimations were normal. Culture of sputum and blood was negative for bacteria and mycobacteria and paired serology for atypical respiratory pathogens (including mycoplasma and legionella) was negative. Arterial blood gases taken breathing room air showed $PaO_2 = 12$ kPa and $PaCO_2 = 3.0$ kPa. A chest radiograph showed coarse reticulonodular bilateral shadowing with consolidation in the antero medial basal segment of the left lower lobe together with a left pleural effusion. The patient was treated for a bacterial chest infection and was treated with IV cefuroxime and oral erythromycin in conventional doses and there was a rapid reduction in fever and dyspnoea. The patient was transfused and was discharged. He was readmitted a month later with a recurrence of symptoms of tiredness and lethargy. Examination revealed lymphoedema of the scrotum and legs.

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Accepted for publication
11 April 1995

Investigations showed Hb = 7.4 g/dl, WBC = 1.5 (neutrophils = 0.6) $\times 10^9/l$ and CD4 count = $0.04 \times 10^9/l$ (3% of total lymphocytes). The patient was transfused with blood and began subcutaneous granulocyte colony stimulating factor (G-CSF) at a dose of 150 mcg four times a week and oral prednisolone 40 mg once daily. He received liposomal doxorubicin 35 mg IV.

He was due for a further dose of liposomal chemotherapy 3 weeks later but at this stage he was admitted once more, clearly unwell, with gross lymphoedema of the legs and lower abdomen with extensive confluent Kaposi's sarcoma. He was pyrexial (temperature 38.8°C) and tachypnoeic. Within the chest there were signs of a large left pleural effusion and a small right pleural effusion. Investigations showed $\text{PaO}_2 = 11.2$ kPa and $\text{PaCO}_2 = 3.2$ kPa (breathing room air). A chest radiograph showed a large pleural effusion with a thick wall containing within it an air-fluid level. There was also a moderate right sided pleural effusion. Cultures of blood, urine, stool and sputum were negative for bacteria, mycobacteria and fungi. The patient was treated with IV cefuroxime, erythromycin and metronidazole in conventional doses. Attempted drainage of the left pleural effusion with a pigtail catheter (19 gauge) achieved drainage of 500 mls of blood stained viscid pus. Laboratory analysis of this showed, on staining, a heavy infiltrate of polymorphs, but no organisms. Culture of the fluid was negative and cytological analysis showed a mixed population of cells including macrophages, neutrophils and mesothelial cells. Following initial drainage the tube blocked. A cardiothoracic surgical opinion was sought and the patient was felt to be a very poor anaesthetic and surgical risk in view of his general condition and the progressive nature of his Kaposi's sarcoma despite chemotherapy. After 6 days of antibiotic therapy the patient remained unwell with a swinging fever and dyspnoea. His oxygen saturations had fallen to 94% breathing air and there was clinical evidence of an increase in size of the left pleural effusion. At this point non surgical treatment was considered and 250 000 units of streptokinase, diluted in 100 ml of normal saline was instilled into the pleural space using the pigtail catheter. The tube was then clamped for 4 hours and the patient asked to lie first on his right side and then on his left side. The tube was then unclamped and over the following 24 hours over 2.5 l of purulent fluid drained. This was associated with a rapid reduction in dyspnoea and lysis of fever. A follow up chest radiograph performed 48 hours after instillation of streptokinase showed almost complete resolution of the left pleural effusion. The chest tube was removed. Despite improvements in fever and dyspnoea there was a general deterioration in the patient's condition. After discussion with his family and carers he declined further active treatment and was treated symptomatically. He died 14 days later; a request for post mortem examination was refused.

Discussion

We gave intrapleural streptokinase to a patient with an empyema that had not resolved with antibiotics and intercostal tube drainage in whom surgery would have been the next therapeutic option. Surgical intervention with pleural decortication carries a significant risk of complications including bacteraemia and there is an associated mortality of between 2 and 33%,^{4 11-13} being highest in those with chronic underlying disease.^{11 13} Our patient had advanced HIV disease with a low CD4 cell count and extensive cutaneous Kaposi's sarcoma that had progressed despite chemotherapy; he was judged to be a poor anaesthetic and surgical risk. We used 250 000 units of streptokinase diluted in 100 ml of normal saline, left in the pleural space for 4 hours, as recommended by Burgh.¹⁴ With this regimen we observed no adverse events in our patient. Fever and chest pain have been reported if higher doses of streptokinase are used or if streptokinase is left in the pleural space for a longer time.^{15 16} Chest discomfort can be reduced or prevented by instilling lignocaine into the pleural space at the same time as the streptokinase.¹⁷ Intrapleural haemorrhage, which has been reported when 500 000 units of streptokinase are left in the pleural space for up to 6 hours⁷ did not occur in our patient.

Two recent studies in non HIV infected individuals with empyema have shown intrapleural streptokinase to be effective.^{9 10} In the first 11 patients with multi loculated empyema refractory to antibiotics and intercostal tube drainage were given 250 000 units of streptokinase intrapleurally for 4 hours.¹⁰ Treatment was effective in eight patients; in contrast to our patient, where a single instillation was effective these patients required up to six instillations (median = three). This suggests that perhaps there is a more intense inflammatory response, with more rapid development of fibrinous loculae, in immunocompetent individuals. Of the three patients in whom streptokinase therapy was ineffective two had a very thickened pleura and required decortication at surgery and one had severe underlying myocarditis and an associated pneumothorax; he died at surgery during attempted decortication. In the second study of 20 patients with parapneumonic effusions five had empyema. Treatment with 250 000 units of streptokinase intrapleurally instilled and left for 3 hours was effective in all five patients. One patient had a high fever ($>39^\circ\text{C}$) with this treatment, otherwise no adverse events were observed.⁹ All patients had reductions in fever and dyspnoea and improvements in levels of discomfort and debility and in chest radiographic appearances. In this study, as in the first, several instillations of streptokinase were necessary to produce an effect (between 3 and 10, median = 6 instillations).⁹ Febrile episodes, systemic fibrinolysis, haemorrhage and anaphylaxis were not seen despite repeated streptokinase exposure. In contrast, this technique was only effective in 12 of 27 patients with empyema in

a study reported by Fraedrich *et al.*¹⁵ However, there were differences in the stage of evolution of pleural effusion, the number of loculations, the amount of pleural fluid and causative organisms compared to the two studies above.^{9 10} In view of the low frequency of adverse reactions to streptokinase, urokinase would only be used, because of its high cost relative to streptokinase, in patients with a past history of allergy to this drug.¹⁸

In conclusion intrapleural streptokinase provides an effective adjunct to initial intercostal tube drainage. Where there is a residual collection of pleural pus streptokinase enhances drainage of fluid which is loculated or is too viscid to be drained by tube thoracostomy alone. The technique is particularly useful in those patients with severe underlying disease such as advanced HIV infection who are poor anaesthetic or surgical risks in whom surgical decortication under general anaesthetic is to be avoided.

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